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ORIGINAL ARTICLE

Changes in Statin Prescription Patterns in Patients Admitted to an Australian Geriatric Subacute Unit

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Background Assessment of demographic and clinical factors influencing the decision of statin discontinuation in the elderly population admitted to subacute geriatric unit. The aim of this study is to assess the clinical factors impacting the decision-making process of statin discontinuation in the elderly.

Methods We retrospectively assessed changes in statin discontinuation and prescription among patients (≥60 years old) discharged from a geriatric evaluation and management unit by reviewing hospital digital medical records at Western Health – The Williamstown Hospital over a 12-month period from 4 February 2012 until 4 February 2013 inclusive. The main outcome of the study was to determine the independent predictors of statin discontinuation using logistic regression analysis.

Results Of the studied population, 46% were already prescribed statins prior to their admission. Statins were discontinued in 17.5% of patients at discharge. Predictors of statin de-prescription included octogenarian status, primary prevention indication, poor functional recovery, residential care facility discharge destination and lower cognitive function. The presence of previous cardiovascular disease history and the burden of comorbidities were not predictors of statin discontinuation.

Abbreviations: CHD, Coronary heart disease; CVD, Cardiovascular disease; ACC/AHA, American College of Cardiology/American Heart Association; GEM, Geriatric Evaluation and Management; TWH, The Williamstown Hospital; MMSE, Mini-Mental State Examination; CCI, Charlson Comorbidity Index; FIM, Functional Independence Measure; PVD, Peripheral vascular disease; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass graft; TIA, Transient ischaemic attack

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Conclusions We observed that factors that conveyed poor prognosis such as advanced age, poor functional recovery, worse cognitive function, being discharged to a residential care facility as well as primary prevention indication for statin prescription are predictors of statin discontinuation in the geriatric unit.

Keywords Statins • Older people • Deprescribing • Octogenarian • Comorbidity

Background

The proportion of older individuals (defined as ≥65 years old) is progressively increasing in Australia, and is projected to represent 24% of the Australian population over the next 20 years [1]. This is partly the result of increased life expectancy due to advances and improved medical treatments for chronic diseases. Coronary heart disease (CHD) is the leading cause of death in Australia contributing to 15% of all deaths and is about 14 times more common in those older than 70 compared to younger patients [2].

The prescription of statins (hydroxymethylglutaryl-CoA reductase inhibitors) in the elderly for primary cardiovascular disease (CVD) prevention remains a contentious subject without clear guideline recommendations [3]. The National Vascular Disease Alliance advises that the prescription of statins as primary prevention for elderly patients should be made according to clinical judgement based on consideration of benefits, potential risks, and co-morbidities [4]. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk [5] acknowledge the limitations of data in the elderly, particularly in the primary prevention setting and advocate for the use of Pooled Cohort Equations to help decision making but also taking into account individualised factors such as comorbidities, safety and goals of care.

Patients with complex medical issues and frailty are frequently admitted to geriatric evaluation and management (GEM) units, which are staffed by multi-disciplinary health care professionals dedicated to patients with multi-dimensional needs associated with ageing. Important objectives of care of GEM units include rationalisation of polypharmacy and to reduce suboptimal prescribing [6]. The primary aim of this study, therefore, was to assess the current hospital-based practices of statin prescription and discontinuation by geriatricians in elderly patients admitted to a large Australian GEM unit.

Methods

Study Population

We retrospectively assessed changes in statin discontinuation and prescription among patients (≥60 years old) by reviewing hospital digital medical records of patients admitted to and discharged from the GEM unit at Western Health – The Williamstown Hospital (TWH) over a 12-month period from 4 February 2012 until 4 February 2013 inclusive. The reviewed data included demographic characteristics, hospital length of stay, discharge destination, cardiovascular disease type and risk factors, dementia, mini-mental state examination (MMSE) score, and statin type on admission and at discharge. The comorbidities included in the Charlson Comorbidity Index (CCI) score [7] were also recorded if documented in the digital medical records and used to calculate the score. The CCI score has been previously validated to predict mortality [8]. The Functional Independence Measure (FIM) score [9] was compared as well on admission and upon discharge to help track the changes in patients' functional status. The FIM score is a reliable, validated score with a total score of 18–126 that is used to track patients' functional status during an admission. It is composed of 18 items, each scored on a seven-point ordinal scale, that assess the motor and cognitive scales of functional capacity including activities of daily living, mobility and social interaction, amongst many others.

Ethics approval was obtained through Western Health Research Office.

Statistical Analysis

Data analysis was performed using the IBM Statistical Package for the Social Sciences program (SPSS) version 22 (Armonk, NY, USA). Binary variables were reported as percentages and compared using a Chi-square test. Mean ± SD was used to summarise normally distributed continuous data. Comparison of means was performed using the unpaired T-test. Univariate logistic regression analysis was performed to select variables that were found to be statistically significant and include them in the multivariate logistic regression model; stepwise backward logistic regression analysis was used to determine the independent predictors of statin discontinuation. A two-tailed p value of less than 0.05 was considered statistically significant.

Results

Patients

This study included 672 patients of whom 309 (46%) were already prescribed statins prior to their GEM admission. Comparison of baseline characteristics between patients already receiving statins on admission with those not prescribed statins (Table 1), demonstrated high rates of CVD risk factors including diabetes, hypertension and dyslipidaemia in the group receiving statins prior to admission (all $p < 0.05$). A secondary prevention indication for CVD prevention was more prevalent among those prescribed statins prior to admission (70% vs. 36%, $p < 0.001$), while patients with a history of dementia (26%

Table 1 Demographic and clinical characteristics of 672 patients discharged from GEM with assessment of statin prescription at time of admission.*

	No Statin (N = 363)	Statin on admission (N = 309)	p Value
Age, years	81.72 ± 8.015	80.92 ± 7.190	0.18
Octogenarians, n (%)	240 (66%)	183 (59%)	*0.065*
Women, n (%)	208 (57%)	199 (64%)	*0.06*
Living at residential care facility, n (%)	9 (2.5%)	5 (2%)	0.436
History of falls, n (%)	188 (52%)	155 (50%)	0.705
Dementia, n (%)	150 (41%)	81 (26%)	***<0.001***
Hypertension, n (%)	242 (67%)	257 (83%)	***<0.001***
Dyslipidaemia, n (%)	69 (19%)	206 (67%)	***<0.001***
Atrial fibrillation, n (%)	88 (24%)	87 (28%)	0.249
Congestive cardiac failure, n (%)	124 (34%)	113 (37%)	0.515
Acute myocardial infarction, n (%)	39 (11%)	71 (23%)	**<0.001**
Coronary heart disease, n (%)	65 (18%)	145 (47%)	***<0.001***
PCI, n (%)	17 (5%)	44 (14%)	***<0.001***
CABG, n (%)	12 (3%)	32 (10%)	***<0.001***
Cerebrovascular disease, n (%)	86 (24%)	130 (42%)	***<0.001***
Plegia, n (%)	28 (8%)	55 (18%)	**<0.001**
Diabetes, n (%)	136 (37%)	159 (51%)	***<0.001***
Complicated	86 (63%)	98 (62%)	***0.02***
Uncomplicated	50 (37%)	61 (38%)	**0.038**
Peripheral vascular disease, n (%)	24 (7%)	34 (11%)	**0.043**
Secondary prevention indication, n (%)	131 (36%)	217 (70%)	**<0.001**
Renal disease, n (%)	106 (29%)	110 (36%)	*0.077*
Rheumatic disease, n (%)	18 (5%)	11 (4%)	0.374
History of smoking, n (%)	136 (37%)	118 (38%)	0.847
Chronic pulmonary disease, n (%)	67 (18%)	50 (16%)	0.438
Mild chronic liver disease, n (%)	19 (5%)	6 (2%)	**0.025**
Moderate to severe chronic liver disease, n (%)	6 (2%)	2 (1%)	0.23
Peptic ulcer, n (%)	19 (5%)	10 (3%)	0.204
Malignancy, n (%)	67 (18%)	43 (14%)	0.113
Metastases, n (%)	14 (4%)	10 (3%)	0.666
CCI score	3.504 ± 2.7904	4.029 ± 2.6948	**0.014**
FIM on admission	71.722 ± 22.4472	72.687 ± 24.8130	0.598

Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; TIA, transient ischaemic attack; PVD, peripheral vascular disease; CCI, Charlson Comorbidity Index; FIM, Functional Independence Measure; MMSE, Mini Mental State Examination.

P values in bold are statistically significant. P values in Italic are ≤0.1.

*Plus-minus values are means ± SD.

vs. 41%, $p < 0.001$), mild chronic liver disease (2% vs. 5%, $p < 0.05$) and octogenarians (59% vs. 66%, $p < 0.065$) were less likely to be prescribed statins. Patients with higher mean CCI score were more likely to have been prescribed a statin prior to admission (4.022.69 vs. 3.504 ± 2.79, $p < 0.05$), predominantly driven by higher prevalence of CHD, CVD and peripheral vascular disease (PVD). Only one participant was initiated on statin therapy in our analysis.

Predictors of Statin Cessation

Upon discharge from GEM, 54 (17.5%) of those who were already prescribed a statin prior to admission (309 patients) had their statin discontinued during their hospital stay (Table 2). Independent multivariable predictors of statin cessation on discharge included octogenarian status (OR 6.1, 95% CI 2.1–17.9), primary prevention indication for statin (OR 5, 95% CI 2.0–12.3), failure of improvement in FIM score during inpatient stay (OR 3.8, 95% CI 1.5–9.5), residential care facility discharge destination (OR 3.26, 95% CI 1.2–8.8) and lower MMSE (OR 1.1, 95% CI 1.02–1.18), all $p < 0.05$ respectively (Figure 1).

Statin Type and Statin Discontinuation

Atorvastatin was prescribed in almost half of the patients, followed by simvastatin, rosuvastatin, pravastatin and fluvastatin. Less than 16% of patients admitted on a statin had maximum strength prescribed as illustrated in Table 3.

Table 2 Demographic and clinical characteristics of patients discharged from GEM with assessment of statin discontinuation.*

	Statin continued (N = 251)	Statin discontinued (N = 54)	p Value
Age, years	80.11 ± 7.279	84.69 ± 5.693	**<0.001**
Octogenarians, n (%)	139 (55%)	41 (76%)	***0.005***
Women, n (%)	165 (66%)	31 (57%)	*0.247*
Length of stay, days	26.588 ± 22.5417	28.025 ± 19.4965	0.664
Discharged to a residential care facility, n (%)	24 (10%)	15 (28%)	**<0.001**
Discharged to high level care facility, n (%)	17 (7%)	11 (20%)	**0.002**
History of falls, n (%)	126 (50%)	28 (51%)	0.847
Dementia, n (%)	61 (24%)	20 (37%)	*0.055*
MMSE	22.97 ± 5.364	18.73 ± 6.785	***<0.001***
Hypertension, n (%)	208 (83%)	45 (83%)	*0.934*
Dyslipidaemia, n (%)	167 (67%)	37 (68%)	*0.779*
Atrial fibrillation, n (%)	73 (29%)	13 (24%)	*0.458*
Congestive cardiac failure, n (%)	89 (35%)	20 (37%)	0.826
Acute myocardial infarction, n (%)	57 (23%)	11 (20%)	0.708
Coronary heart disease, n (%)	120 (48%)	22 (41%)	0.345
PCI, n (%)	35 (14%)	7 (13%)	0.849
CABG, n (%)	27 (11%)	5 (9%)	0.745
Cerebrovascular disease, n (%)	112 (45%)	16 (30%)	**0.043**
Plegia, n (%)	47 (19%)	7 (13%)	0.314
Diabetes, n (%)	128 (51%)	28 (52%)	0.909
Complicated	74 (58%)	22 (41%)	*0.106*
Uncomplicated	54 (42%)	6 (11%)	*0.081*
Peripheral vascular disease, n (%)	29 (12%)	3 (6%)	*0.192*
Primary prevention indication, n (%)	67 (27%)	25 (46%)	**0.004**
Renal disease, n (%)	85 (34%)	24 (44%)	0.141
Rheumatic disease, n (%)	9 (4%)	2 (4%)	0.966
History of smoking, n (%)	92 (37%)	22 (41%)	0.576
Chronic pulmonary disease, n (%)	39 (16%)	8 (15%)	0.894
Mild chronic liver disease, n (%)	4 (2%)	2 (4%)	0.311
Moderate to severe chronic liver disease, n (%)	1 (0.4%)	1 (2%)	0.230
Peptic ulcer, n (%)	8 (3%)	2 (4%)	0.847
Malignancy, n (%)	34 (14%)	8 (15%)	*0.806*
Metastases, n (%)	7 (3%)	3 (6%)	0.3
CCI score	3.93 ± 2.632	4.31 ± 2.893	0.342
FIM score on admission	74.04 ± 25.069	66.68 ± 23.481	**0.05**
FIM score on discharge	90.42 ± 26.382	75.19 ± 29.005	**<0.001**
Failed to improve FIM score during admission	43 (17%)	21 (39%)	**<0.001**

Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; TIA, transient ischaemic attack; PVD, peripheral vascular disease; CCI, Charlson Comorbidity Index; FIM, Functional Independence Measure; MMSE, Mini Mental State Examination.

P values in bold are statistically significant. P values in Italic are ≤0.1.

*Plus-minus values are means ± SD.

Discussion

In our study, we observed that patients admitted to the GEM unit were more likely to have their statin medication discontinued if they were octogenarians, had a primary prevention indication for statin prescription, had no improvement in their FIM score during inpatient stay, discharged to a residential care facility or had worse MMSE score independent of other demographic and clinical variables.

The higher likelihood of statin cessation when patients are discharged to a residential care facility or with advancing age could be related to the patients' perceived poor prognostic outcome or frailty. Observational studies have shown that older, frail individuals are at an increased risk of medication-related adverse events including statins [10,11]. Therefore, reducing polypharmacy by minimising the use of unnecessary preventive medications may be appropriate in this population and is one of the many aims of GEM units. Our

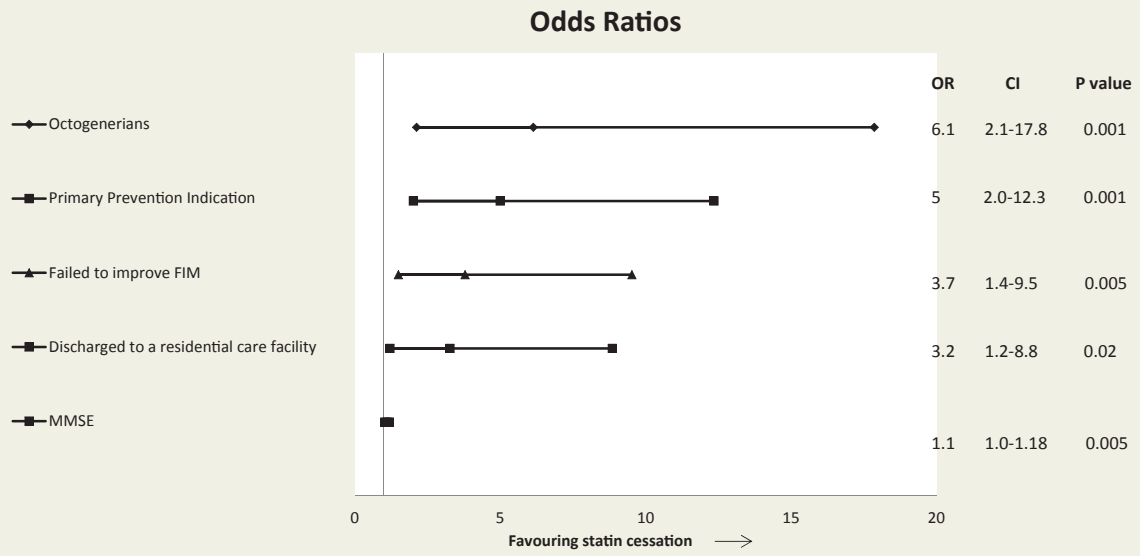

Figure 1 Independent predictors of statin discontinuation.

findings are similar to the study conducted by Gnjidic and colleagues [12], which identified advancing age as a predictor of statin discontinuation in an Australian population residing in residential care facilities. Likewise, Sheppard et al. also reported an association between advancing age and statin non-prescription particularly for primary prevention [13]. A study by Nishtala and colleagues [14] in New Zealand identified limited prognosis as the major factor in statin discontinuation regardless of the indication.

The increased burden of cardiovascular comorbidities in the elderly can lead to polypharmacy and may result in numerous drug-related adverse effects and drug interactions [15] if guideline directed medical therapy is applied without rational prescribing. In addition, clinicians might be hesitant to discontinue a medication that is guideline recommended, particularly relating to CVD given the well-published guidelines on CVD prevention, although there remains a paucity of data on the effects of statins in elderly patients. The decision to de-prescribe a medication is complex and takes into account several factors, including the strength of clinical indication, patient complexity and the shared management with other health care providers. It is known that clinicians of different specialities manage CVD conditions differently [16], complicating the decision to start or discontinue a medication. While several frameworks have been proposed for medication discontinuation [17,18], a universal paradigm that takes into account the complexity and heterogeneity of the elderly population is yet to be developed.

Previous clinical studies have supported the safety of short periods of discontinuation in patients with stable CHD [19], however, longer durations of discontinuation have not been well-studied. A randomised controlled trial by Kutner and colleagues [20] evaluated the outcomes of statin discontinuation in patients with advanced disease and limited prognosis. The results of this study support the safety and potentially improved quality of life with statin discontinuation, providing much needed information in those with a guarded prognosis. Patients with intermediate prognosis, however, were not investigated in this study.

A primary prevention indication of statin therapy was an independent predictor of in-hospital cessation. This finding is in accord with previous published studies [21,22]. An important explanation is the perceived limited benefit from statin therapy in elderly patients with no prior history of CVD such as myocardial infarction or stroke [23–25]. Indeed, it is well known from patients enrolled in the Framingham

Table 3 **Statins prescribed at admission and discharge.**

Type of statin	Admitted on statin (n = 309)	Maximum dose statin (n = 309)	Statin ceased (n = 54)
Atorvastatin	147 (48%)	30 (10%)	21 (38.8%)
Simvastatin	97 (31%)	11 (4%)	19 (35.1%)
Rosuvastatin	49 (16%)	4 (1%)	12 (22.2%)
Pravastatin	12 (4%)	1 (0.3%)	3 (5.5%)
Fluvastatin	1 (0.3%)	0	0

Heart study that the association of CVD with cholesterol levels in the elderly is weak, particularly at ages 70 years and beyond [26]. Moreover, the exclusion of the elderly population from statin trials [27], together with the questionable association of cholesterol and mortality in the elderly, the so-called lipid paradox [26], pose an important clinical dilemma when considering statin prescription in the primary prevention setting where the magnitude of benefit is likely small versus the economic and drug-related adverse effects and interactions. However, a meta-analysis by Teng and colleagues [28], observed reductions in major adverse cardiovascular events in the elderly who were prescribed statins without a significant increase in adverse events. Nevertheless, a significant limitation of this analysis was the significant heterogeneity of the studied population (Q test $p = 0.028$). In addition, the numbers needed to treat over 3.5 years to prevent one event in this meta-analysis was high for cardiac disease (NNT = 83) and even higher for cerebrovascular disease (NNT = 142) underscoring the relatively modest benefit of statin prescription in the elderly [29].

Based on the 2013 ACC/AHA guidelines [5], a significant proportion of the healthy elderly population would qualify for statin therapy as primary prevention by virtue of their age alone (white men at age 63 and white women at age 71) [30]. However, this approach has important limitations including a lack of consideration of co-morbidities, frailty, and other markers of CVD risk. A more individualised approach was proposed by Mortensen and colleagues in their prospective cohort study [31], which re-stratified patients based on non-invasive assessment of sub-clinical atherosclerosis utilising coronary artery calcium and carotid plaque burden. Utilising a calcium score of 0 to down-classify statin-eligible patients with 10-year atherosclerotic cardiovascular disease risk $\geq$7.5% to statin-ineligible improved the specificity substantially from 15% to 37% with very little change in sensitivity of the Pooled Cohort Equations used to assess CVD risk. This individualised approach may help minimise unnecessary statin prescriptions, improve quality of life as well as be cost saving to the health care system.

There was a significant difference in the CCI score between the group that had their statins discontinued and those who were continued on statins (3.9 ± 2.6 vs. 4.3 ± 2.8, $p = 0.34$). This could be explained by the high CCI score in the group that was admitted on statins given the high prevalence of CVD risk factors. Charlson Comorbidity Index score, however, was not an independent predictor of statin cessation on multivariate analysis. Interestingly, those in the statin discontinuation vs. continued group had worse FIM score on discharge (90.4 ± 26.3 vs. 75.1 ± 29.0, $p < 0.001$). Failure of functional status recovery as assessed by the FIM score change during GEM unit stay predicted statin cessation (OR 3.7, 95% CI 1.4–9.5, $p = 0.001$). Similarly, a lower mean MMSE score independently predicted statin cessation (OR 1.1, 95% CI 1.0–1.18, $p = 0.005$) which suggests that functional status at discharge and cognitive function had a greater bearing on medication deprescription decision than the burden of comorbidities.

Our study has important clinical implications. To our knowledge, this is the first Australian study to investigate statin cessation in the GEM unit setting. Given the annual high cost of statins for both patients and the health care system, further research is needed to evaluate any differences in clinical outcomes between elderly patients with intermediate prognosis prescribed statins for secondary prevention versus primary prevention indication. Such research should ideally also incorporate health economics as well.

There are several limitations to this study that warrant consideration when interpreting the results. First, this was a single-centre, retrospective, non-randomised, observational analysis. Second, we only reviewed medications on admission to GEM unit, and therefore, might have missed any statins started or ceased during admission to the acute ward prior to transfer to GEM unit. Third, our results refer to the Australian population and, thus, might not be generalisable to European or US populations. Fourth, data pertaining to the particular clinician responsible for care (and there were many in our busy Geriatric Unit) was not collected in our study. Furthermore, there were likely other members in our multidisciplinary team who might have influenced the decision to cease a medication including registrars and pharmacists. The effect of treating team decision to continue or discontinue statin would be difficult to assess in our retrospective study. Finally, we did not perform correlation of statin use or discontinuation with clinical outcomes or quality of life measures as this would require a much larger sample size and prospective follow-up.

Conclusion

In our study, we observed that factors that conveyed poor prognosis such as octogenarian status, poor FIM score recovery during their in-patient stay, and worse MMSE score as well as a less compelling indication for CVD prevention were independent predictors for statin cessation in elderly patients discharged from a GEM unit. Changes in statin prescription among the elderly require further research and may need to be individualised.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2017.12.009.

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